

Listing of Claims

1.-11. Canceled

12. (Currently amended) A method for modulating expression of a target gene product in a cell in culture that contains a target gene under control of one or more regulatory elements,

said method comprising contacting the cell in culture under suitable conditions with one or more regulatory agents attached to a translocating polypeptide, whereby the one or more regulatory agents are translocated into the cell in culture and interact therein with the one or more regulatory elements, thereby modulating expression of the target gene product by the cell wherein the translocating polypeptide exhibits receptor-independent and energy-free penetration of cell membranes, wherein the cell does not have a cell wall; and wherein the one or more regulatory agents include a recombinase.

13. (Currently amended) The method according to claim 12 wherein the cell in culture is a mammalian, ~~yeast~~, or insect cell.

14. Canceled

15. (Original) The method according to claim 12 wherein the translocating polypeptide is a VP22 polypeptide, Antp, or Protein H.

16. (Original) The method according to claim 12 wherein the translocating polypeptide is a VP22 polypeptide.

17-20. (Canceled)

21. (Currently amended) A method for modulating expression of a target gene product in a cell in culture that contains a target gene under control of one or more regulatory elements,

said method comprising contacting the cell under suitable conditions with one or more regulatory agents attached to a translocating polypeptide, whereby the one or more regulatory agents are translocated into the cell in culture and interact therein with the one or more regulatory elements, thereby modulating expression of the target gene product by the cell wherein the translocating polypeptide exhibits receptor-independent and energy-free penetration of cell membranes, wherein the cell does not have a cell wall; wherein the one or more regulatory elements includes a promoter and wherein the one or more regulatory agents include a polymerase specific for the promoter.

22. (Original) The method according to claim 21 wherein the polymerase is T7 RNA polymerase and the promoter is a T7 promoter.

23. (Currently amended) A method for modulating expression of a target gene product in a cell in culture that contains a target gene under control of one or more regulatory elements,

said method comprising contacting the cell under suitable conditions with one or more regulatory agents attached to a translocating polypeptide, whereby the one or more regulatory agents are translocated into the cell in culture and interact therein with the one or more regulatory elements, thereby modulating expression of the target gene product by the cell wherein the translocating polypeptide exhibits receptor-independent and energy-free penetration of cell membranes, wherein the cell does not have a cell wall; wherein the one or more regulatory agents include an HIV Rev protein and the one or more regulatory elements include the HIV Rev response element (RRE).

24. Canceled.

25. (Previously Presented) The method according to claim 12 wherein the one or more regulatory agents and the translocating polypeptide are covalently attached.

26. (Previously Presented) The method according to claim 12 wherein the one or more regulatory agents and the translocating polypeptide are attached by a linker.

27. (Original) The method according to claim 26 wherein the linker comprises one or more disulfide bonds, salicylhydroxamic acid (SHA), phenylboronic acid (PBA), a SHA-NHS ester, or a combination thereof.

28. (Previously Presented) The method according to claim 12 wherein the translocating polypeptide and the one or more regulatory agents are units of a fusion protein.

29-30. (Canceled)

31. (Previously Presented) The method according to claim 12 wherein the translocating polypeptide and the one or more regulatory agents are linked by a biotin-streptavidin complex or the *E. Coli* single stranded DNA binding protein.

32. (Presented Previously) The method according to claim 12 wherein the one or more regulatory agents include a site-specific recombinase, the cell contains a first nucleic acid with at least one site-specific genomic recombination site, and a second nucleic acid containing the target gene and at least one site-specific recombination site wherein the recombinase is specific for the recombination sites, and wherein translocation of the site-specific recombinase causes recombination between the site-specific recombination sites resulting in stable integration of the target gene into the genome of the cell at the genomic recombination site.

33. (Previously Presented) The method according to claim 32 wherein the recombinase is a member of the family of site-specific recombinases selected from the groups consisting of the integrase family of site-specific recombinases and the resolvase/invertase family of site-specific recombinases.

34. (Presently Presented) The method according to claim 32 wherein the site-specific recombination sites are *frt* sites and the site-specific recombinase is Flp or the site-

specific recombination sites are lox recombination sites and the site-specific recombinase is Cre.

35. (Currently Amended) The method according to claim 12 wherein the one or more regulatory agents include a site-specific recombinase which excises ~~wherein the one or more regulatory elements of the target gene are flanked by site-specific recombination sites wherein the site-specific recombinase is specific for the flanking recombination sites, wherein translocation of the site-specific recombinase causes recombination of the flanking site-specific recombination sites,~~ thereby modulating expression of the target gene product.

36. (Currently Amended) The method according to claim 35 wherein ~~the flanking recombination sites are *f/t* sites and the site-specific recombinase is Flp or the flanking recombination sites are lox sites and the site-specific recombinase is Cre.~~

37. Canceled

38. (Original) The method according to claim 12 wherein the target gene is a reporter gene.

39. (Original) The method according to claim 12 wherein the target gene is contained within a polynucleotide that further encodes a protein tag.

40. (Original) The method according to claim 12 wherein the target gene encodes a toxic protein.

41. (Original) The method according to claim 39 wherein the protein tag is a myc epitope, a fluorescent peptide, or a poly His tag, or a combination of any two or more thereof.

42.-50. (Canceled)

51. (Currently Amended) The method of claim 12 wherein the cell in culture is a eukaryotic cell.
52. (Previously Presented) The method according to claim 12 wherein the one or more regulatory agents and the translocating polypeptide are non-covalently attached.
53. (Currently Amended) The method according to claim 12 wherein the recombinase is a ~~site-specific~~ site-specific recombinase.
54. (Previously Presented) The method of claim 53 wherein the site-specific recombinase is a member of a family of site-specific recombinases selected from the group consisting of the integrase family of site-specific recombinases and the resolvase/invertase family of site-specific recombinases.
55. (Currently Amended) The method according to claim 54 wherein the site-specific recombination sites are *frt* sites and the site-specific recombinase is Flp or the site-specific recombination ~~recombinase~~ sites are *lox* recombination sites and the site-specific recombinase is Cre.
56. (Canceled)
57. (Currently Amended) The method according to claim ~~56~~ 58 wherein the regulatory element is a promoter.
58. (Currently Amended) ~~The method according to claim 56~~ A method for modulating expression of a target gene product in a cell in culture that contains a target gene under control of one or more regulatory elements,
said method comprising contacting the cell under suitable conditions with one or more regulatory agents attached to a translocating polypeptide, whereby the one or more regulatory agents are translocated into the cell in culture and interact therein with the one or more regulatory elements, thereby modulating expression of the target gene product by

the cell wherein the translocating polypeptide exhibits receptor-independent and energy-free penetration of cell membranes, wherein the cell does not have a cell wall; and wherein the one or more regulatory agents include a DNA-binding protein wherein the DNA-binding protein has a DNA-binding domain selected from the group consisting of a DNA-binding domain of a member of the steroid/thyroid hormone nuclear receptor superfamily, the GAL4DNA binding domain, a DNA-binding domain of a homeobox protein, a DNA-binding domain of a zinc finger protein, a DNA-binding domain of a hormone receptor, a DNA-binding domain of a helix-turn-helix protein, a DNA-binding protein of a basic-Zip protein, a DNA binding protein of a β -ribbon factor and a DNA-binding domain of a Tet operon.

59. (Previously Presented) The method of claim 58 wherein the DNA-binding domain is that of Seq ID No:4.

60. (Currently Amended) ~~The method according to claim 56~~ A method for modulating expression of a target gene product in a cell in culture that contains a target gene under control of one or more regulatory elements,

said method comprising contacting the cell under suitable conditions with one or more regulatory agents attached to a translocating polypeptide, whereby the one or more regulatory agents are translocated into the cell in culture and interact therein with the one or more regulatory elements, thereby modulating expression of the target gene product by the cell wherein the translocating polypeptide exhibits receptor-independent and energy-free penetration of cell membranes, wherein the cell does not have a cell wall; and wherein the one or more regulatory agents include a DNA-binding protein wherein the DNA-binding protein is a histone 1(H1) protein or a non-histone protein HMG-17.

61. (Currently Amended) The method according to claim ~~56~~ 12 wherein ~~the DNA-binding protein~~ the translocating polypeptide and the one or more regulatory agents are linked by a Vaccinia ~~is a DNA topoisomerase I linker.~~

62. (Canceled)

63. (New) The method according to claim 21 wherein the translocating polypeptide is a VP22 polypeptide.
64. (New) The method according to claim 23 herein the translocating polypeptide is a VP22 polypeptide.
65. (New) The method according to claim 58 wherein the translocating polypeptide is a VP22 polypeptide.
66. (New) The method according to claim 21 wherein the translocating polypeptide and the one or more regulatory agents are units of a fusion protein.
67. (New) The method according to claim 23 wherein the translocating polypeptide and the one or more regulatory agents are units of a fusion protein.
68. (New) The method according to claim 58 wherein the translocating polypeptide and the one or more regulatory agents are units of a fusion protein.